

A<sup>10</sup>

1 125. (Amended) Use according to claim 124, where one of the target genes is the PKR  
2 gene.

*[Handwritten signature]*

REMARKS

The application has been amended to conform to U.S. practice. The claims have been amended to eliminate multiple dependency.

STATEMENT UNDER 37 CFR 1.821(f)

I, John P. Murtaugh, hereby state that the information recorded in computer readable form is identical to the written sequence listing.

Please charge any fees and credit any overpayments under 37 CFR 1. 16 and 1. 17 during the entire pendency of this application to our Deposit Account No. 16-0820, Order No. 33796.

If any fees are required by this communication, please charge such fees to our Deposit Account No. 16-0820, Order No. 33796.

Respectfully submitted,  
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Date: 7-20-01

INDICATION OF REVISIONS TO THE CLAIMS  
IN U.S. NATIONAL PHASE OF PCT/DE00/00244

1 3. (Amended) Method according to [either of the preceding  
2 claims] claim 1, where the dsRNA is enclosed by natural viral  
3 capsids or by chemically or enzymatically produced artificial  
4 capsids or structures derived therefrom.

1 4. (Amended) Method according to [one of the preceding  
2 claims] claim 1, where the target gene is expressed in  
3 eukaryotic cells.

1 5. (Amended) Method according to [one of the preceding  
2 claims] claim 1, where the target gene is selected from the  
3 following group: oncogene, cytokin gene, Id-protein gene,  
4 development gene, prion gene.

1 6. (Amended) Method according to [one of the preceding  
2 claims] claim 1, where the target gene is expressed in pathogenic organisms, preferably in  
3 plasmodia.

1 7. (Amended) Method according to [one of the preceding claims] claim 1, where the  
2 target gene is part of a virus or viroid.

1 10. (Amended) Method according to [one of the preceding claims] claim 1, where  
2 segments of the dsRNA are in double-stranded form.

1 11. (Amended) Method according to [one of the preceding claims] claim 1, where the  
2 ends of the dsRNA are modified in order to counteract degradation in the cell or dissociation  
3 into the single strands.

1 12. (Amended) Method according to [one of the preceding claims] claim 1, where the  
2 cohesion of the double-stranded structure, which is caused by the complementary nucleotide

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2 chemical linkage is formed by thiophosphoryl groups provided at the ends of the double-  
3 stranded structure.

1 21. (Amended) Method according to [one of the preceding claims] claim 1, where the  
2 chemical linkage at the ends of the double-stranded structure is formed by triple-helix bonds.

1 22. (Amended) Method according to [one of the preceding claims] claim 1, where at least  
2 one 2'-hydroxyl group of the nucleotides of the dsRNA in the double-stranded structure is  
3 replaced by a chemical group, preferably a 2'-amino or a 2'-methyl group.

1 23. (Amended) Method according to [one of the preceding claims] claim 1, where at least  
2 one nucleotide in at least one strand of the double-stranded structure is a locked nucleotide  
3 with a sugar ring which is chemically modified, preferably by a 2'-O, 4'-C-methylene bridge.

1 24. (Amended) Method according to [one of the preceding claims] claim 1, where the  
2 dsRNA is bound to, associated with or surrounded by, at least one viral coat protein which  
3 originates from a virus, is derived therefrom or has been prepared synthetically.

1 25. (Amended) Method according to [one of the preceding claims] claim 1, where the coat  
2 protein is derived from polyomavirus.

1 26. (Amended) Method according to [one of the preceding claims] claim 1, where the coat  
2 protein contains the polyomavirus virus protein 1 (VP1) and/or virus protein 2 (VP2).

1 27. (Amended) Method according to [one of the preceding claims] claim 1, where, when a  
2 capsid or capsid-type structure is formed from the coat protein, one side faces the interior of  
3 the capsid or capsid-type structure.

1 28. (Amended) Method according to [one of the preceding claims] claim 1, where one  
2 strand of the dsRNA is complementary to the primary or processed RNA transcript of the  
3 target gene.



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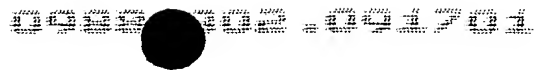
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least one 2'-hydroxyl group of the nucleotides of the dsRNA in the double-stranded structure is replaced by a chemical group, preferably a 2'-amino or a 2'-methyl group.

78. (Amended) Active ingredient according to [one of claims 63 to 77] claim 63, where at least one nucleotides at least one strand of the double-stranded structure is a locked nucleotide with a sugar ring which is chemically modified, preferably by a 2'-O, 4'-C-methylene bridge.

79. (Amended) Active ingredient according to [one of claims 63 to 78] claim 63, where one strand of the dsRNA is complementary to the primary or processed RNA transcript of the target gene.

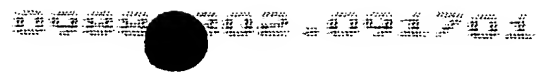
80. (Amended) Active ingredient according to [one of claims 63 to 79] claim 63, where at least two dsRNAs which differ from each other are contained in the active ingredient, where at least segments of one strand of each dsRNA are complementary to in each case one of at least two different target genes.

83. (Amended) Use according to [either of claims 81 or 82] claim 81, where the dsRNA is enclosed by natural viral capsids or by chemically or enzymatically produced artificial capsids or structures derived therefrom.

84. (Amended) Use according to [one of claims 81 to 83] claim 81, where the target gene can be expressed in eukaryotic cells.

85. (Amended) Use according to [one of claims 81 to 84] claim 81, where the target gene is selected from the following group: oncogene, cytokin gene, Id-protein gene, development gene, prion gene.

86. (Amended) Use according to [one of claims 81 to 85] claim 81, where the target gene can be expressed in pathogenic organisms, preferably in plasmodia.



1 87. (Amended) Use according to [one of claims 81 to 86] claim 81, where the target gene  
2 is part of a virus or viroid.

1 90. (Amended) Use according to [one of claims 81 to 89] claim 81, where segments of the  
2 dsRNA are in double-stranded form.

1 91. (Amended) Use according to [one of claims 81 to 90] claim 81, where the ends of the  
2 dsRNA are modified in order to counteract degradation in the cell or dissociation into the  
3 single strands.

1 92. (Amended) Use according to [one of claims 81 to 91] claim 81, where the cohesion of  
2 the double-stranded structure, which is caused by the complementary nucleotide pairs, is  
3 increased by at least one, preferably two, further chemical linkage(s).

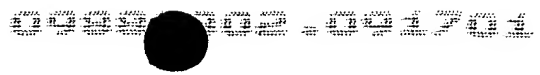
1 93. (Amended) Use according to [one of claims 81 to 92] claim 81, where the chemical  
2 linkage is formed by a covalent or ionic bond, a hydrogen bond, hydrophobic interactions,  
3 preferably van-der-Waals or stacking interactions, or by metal-ion coordination.

1 94. (Amended) Use according to [one of claims 81 to 93] claim 81, where the chemical  
2 linkage is generated at at least one, preferably both, ends of the double-stranded structure.

1 95. (Amended) Use according to [one of claims 81 to 94] claim 81, where the chemical  
2 linkage is formed by means of one or more compound groups, the compound groups  
3 preferably being poly(oxyphosphinicoxy-1,3-propanediol) and/or polyethylene glycol  
4 chains.

1 96. (Amended) Use according to [one of claims 81 to 95] claim 81, where the chemical  
2 linkage is formed by purine analogs used in the double-stranded structure in place of purines.

1 97. (Amended) Use according to [one of claims 81 to 96] claim 81, where the chemical  
2 linkage is formed by azabenzene units introduced into the double-stranded structure.



- 1 98. (Amended) Use according to [one of claims 81 to 97] claim 81, where the chemical  
2 linkage is formed by branched nucleotide analogs used in the double-stranded structure in  
3 place of nucleotides.
- 1 99. (Amended) Use according to [one of claims 81 to 98] claim 81, where at least one of  
2 the following groups is used for generating the chemical linkage: methylene blue;  
3 bifunctional groups, preferably bis(2-chloroethyl)amine; N-acetyl-N'-(p-  
4 glyoxylbenzoyl)cystamine; 4-thiouracil; psoralene.
- 1 100. (Amended) Use according to [one of claims 81 to 99] claim 81, where the chemical  
2 linkage is formed by thiophosphoryl groups attached to the ends of the double-stranded  
3 structure.
- 1 101. (Amended) Use according to [one of claims 81 to 100] claim 81, where the chemical  
2 linkage at the ends of the double-stranded structure is formed by triple-helix bonds.
- 1 102. (Amended) Use according to [one of claims 81 to 101] claim 81, where at least one  
2 2'-hydroxyl group of the nucleotides of the dsRNA in the double-stranded structure is  
3 replaced by a chemical group, preferably a 2'-amino or a 2'-methyl group.
- 1 103. (Amended) Use according to [one of claims 81 to 102] claim 81, where at least one  
2 nucleotide in at least one strand of the double-stranded structure is a locked nucleotide with a  
3 sugar ring which is chemically modified, preferably by a 2'-O, 4'-C-methylene bridge.
- 1 104. (Amended) Use according to [one of claims 81 to 103] claim 81, where the dsRNA is  
2 bound to, associated with or surrounded by, at least one viral coat protein which originates  
3 from a virus, is derived therefrom or has been prepared synthetically.
- 1 105. (Amended) Use according to [one of claims 81 to 104] claim 81, where the coat  
2 protein is derived from polyomavirus.
- 1 106. (Amended) Use according to [one of claims 81 to 105] claim 81, where the coat

protein contains the polyomavirus virus protein 1 (VP1) and/or virus protein 2 (VP2).

107. (Amended) Use according to [one of claims 81 to 106] claim 81, where, when a capsid or capsid-type structure is formed from the coat protein, one side faces the interior of the capsid or capsid-type structure.

108. (Amended) Use according to [one of claims 81 to 107] claim 81, where one strand of the dsRNA is complementary to the primary or processed RNA transcript of the target gene.

109. (Amended) Use according to [one of claims 81 to 108] claim 81, where the cell is a vertebrate cell or a human cell.

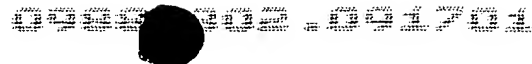
110. (Amended) Use according to [one of claims 81 to 109] claim 81, where at least two dsRNAs which differ from each other are used, where at least segments of one strand of each dsRNA are complementary to in each case one of at least two different target genes.

112. (Amended) Use according to [one of claims 81 to 111] claim 81, where the medicament is injectable into the blood-stream or into the interstitium of the organism to undergo therapy.

113. (Amended) Use according to [one of claims 81 to 112] claim 81, where the dsRNA is taken up into bacteria or micro-organisms.

116. (Amended) Use according to claim 114 [or 115], where the target gene is selected from the following group: oncogene, cytokin gene, Id-protein gene, development gene, prion gene.

117. (Amended) Use according to [one of claims 114 to 116] claim 114, where the target gene can be expressed in pathogenic organisms, preferably in plasmodia.



1 118. (Amended) Use according to [one of claims 114 to 117]  
2 claim 114, where the target gene is part of a virus or viroid.

1 121. (Amended) Use according to [one of claims 114 to 120]  
2 claim 114, where segments of the dsRNA are in double-stranded  
3 form.

1 122. (Amended) Use according to [one of claims 114 to 121]  
2 claim 114, where one strand of the dsRNA is complementary to  
3 the primary or processed RNA transcript of the target gene.

1 123. (Amended) Use according to [one of claims 114 to 122]  
2 claim 114, where the cell is a vertebrate cell or a human  
3 cell.

1 124. (Amended) Use according to [one of claims 114 to 123]  
2 claim 114, where at least two dsRNAs which differ from each  
3 other are used, where at least segments of one strand of each  
4 dsRNA are complementary to in each case one of at least two  
5 different target genes.

1 125. (Amended) Use according to claim [125] 124, where one of  
2 the target genes is the PKR gene.